REMARKS

In view of the above amendments and the following remarks reconsideration of the outstanding office action is respectfully traversed.

The July 29, 2003, interview between Examiner Hutson, inventor Steven Goldman, M.D., Ph.D., and applicants' undersigned attorney is gratefully acknowledged. The substance of that interview is set forth below.

The rejection of claims 25, 26, and 29 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 25, 26, and 29 under 35 U.S.C. § 112 (1st para.) for failure to satisfy the written description requirement is respectfully traversed in view of the above amendments.

The rejection of claims 25, 26, and 29 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed in view of the above amendments.

The rejection of claims 25, 26, and 29 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,361,996 to Rao, et. al., ("Rao") is respectfully traversed.

Rao discloses multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells. The astrocyte/oligodendrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into astrocytes and oligodendrocytes but not neurons. Rao characterizes these cells as "multipotential intermediate precursor cells restricted to glial lineages" (emphasis added)(col. 23, lines 1-5), thereby suggesting that they are distinct from more committed precursors or progenitor cells. Indeed, Rao et al., "Glial-Restricted Precursors are Derived From Multipotential Neuroepithelial Stem Cells," *Devel. Biol.* 188:48-63 (1997) clearly demonstrate the strong astrocytic bias of their cells which generated few, if any, oligodendrocytes (See attached Third Declaration of Steven A. Goldman Under 37 C.F.R. § 1.132 ("Third Goldman Declaration") ¶ 5). Since Rao's astrocyte/oligodendrocyte precursor cells are not committed to formation of oligodendrocytes and, therefore, are in a less differentiated state than the claimed oligodendrocyte progenitor cells, it is apparent that this reference in no way suggests the claimed invention.

In addition to failing to teach the claimed oligodendrocyte progenitor cells, Rao also worked with cells from rats rather than from humans, as required by the claimed invention. For substantially the same reasons pointed out in the June 10, 2002, Preliminary Amendment, based on the Declaration of Steven A. Goldman under 37 C.F.R. § 1.132 ("First Goldman Declaration"), the

teachings of Rao are not pertinent to the claimed invention. Although that declaration was directed to U.S. Patent No. 5,276,145 to Bottenstein ("Bottenstein"), the issues regarding that reference are substantially the same as those pertaining to Rao. In particular, there are fundamental differences between the biology of rat and human oligodendrocyte progenitor cells (First Goldman Declaration ¶ 7). Furthermore, there are fundamental differences between the lineage restriction and potential of neonatal and adult oligodendrocyte progenitor cells (Third Goldman Declaration ¶ 6). These biological differences between both rat and human and perinatal and adult progenitor cells were not recognized by either Rao or Bottenstein, whose cells were restricted to neonatal rodent derivation (First Goldman Declaration ¶ 7; Third Goldman Declaration ¶ 6). Whereas rat oligodendrocytes appear to retain mitotic potential, human oligodendrocytes do not (First Goldman Declaration ¶ 7). See Kirschenbaum et al., "*In Vitro* Neuronal Production and Differentiation by Precursor Cells Derived from the Adult Human Forebrain," *Cerebral Cortex* 6:576-89 (1994) which has been previously applied against the claims. As a result, the oligodendrocyte progenitor cells of the rat brain cannot be considered homologous to its human counterpart (Id.). In particular, methods that permit the selective extraction and/or growth of oligodendrocyte progenitors from the rat brain do not differentiate between oligodendrocyte progenitor cells and mature oligodendrocytes able to re-enter the mitotic cycle (Id.). In humans, these constitute two discrete phenotypes, lineally related but temporally distinct (Id.). The present invention teaches the selective acquisition of a highly enriched – to virtual purity - mitotically-competent oligodendrocyte progenitor cell pool, operationally separate and distinct from post-mitotic or mature oligodendrocytes (Id.).

Figures 1 and 2 of Rao show his astrocyte/oligodendrocyte precursor cells differentiating directly to astrocytes and, to a much lesser extent, to oligodendrocytes with these mature cell types being characterized by various markers. It may be accurate to characterize rat oligodendrocytes and oligodendrocyte progenitors together at least with regard to their markers, because those markers are similar. Specifically, rat oligodendrocyte progenitors and oligodendrocytes both express the antigenic marker recognized by monoclonal antibody O4 (Third Goldman Declaration ¶ 7). In contrast, this marker is expressed by human oligodendrocytes and their immature forms, but NOT by mitotic oligodendrocyte progenitor cells (Id.). As a result, human oligodendrocyte progenitor cells cannot be acquired through the use of O4 as a selection marker, and O4-defined human oligodendroglial cells cannot act as mitotically-competent progenitor cells (Id.). This is in sharp distinction to the rat brain, in which the use of this marker can identify oligodendrocyte progenitors. Neither Rao nor Bottenstein recognized the non-applicability of this marker to the separation of human oligodendrocyte progenitor cells (Id.). In humans, mitotic cells

biased strongly towards the oligodendrocyte lineage are instead recognized by the antigenic phenotype $O4^-$/PSA-$NCAM^-$/$A2B5^+$, which comprise a distinct subpopulation in which the CNP2 (i.e. cyclic nucleotide phosphodiesterase 2) promoter is transcriptionally activated (Id.).

Rao and Bottenstein are directed at the enrichment of glial progenitor cells from newborn rat brain (See First Goldman Declaration ¶ 8). Newborns have an abundant population of still-developing oligodendrocyte progenitor cells that may constitute a significant fraction of all of the cells in neonatal brain tissue (Id.). Bottenstein reported that >30% of the cells of its tissue dissociates expressed the marker of this phenotype (Id.). With the addition of B104 conditioned media and the neural progenitor regulatory factor, this fraction increased to just over 40% (Id.). The nature of these cells is that of a still-mixed pool, in that the following populations appear to be represented by Bottenstein's data: astrocytes, oligodendrocytes, and a mixture of neural lineage cells of widely different developmental stages (Id.). Worse, the remaining cells are of an undesired phenotype.

In contrast to the cells acquired from newborn rats using the Bottenstein protocol, the present invention is achieved with a procedure that permits, in both young and old humans, the selective extraction of progenitor cells strongly biased to oligodendrocytic phenotype, and allows the purification of these cells, including those from tissues in which they are scarce (e.g., postnatal and adult brain tissues harboring <1% of the desired oligodendrocyte progenitor cell type) (First Goldman Declaration ¶9). In Example 5 of the present patent application, the virtual purification of oligodendrocyte progenitor cells from tissues with a P/CNP2 promoter-targeted FACS-defined incidence of <1% was reported (Id.). This constituted a far greater enrichment of the oligodendrocyte progenitor cell (i.e. 170-fold) than that achieved by Bottenstein (i.e. less than 1.5-fold) and yields a far more pure product of oligodendrocyte progenitor cells (Id.). The product of the present invention is thus not only purer, but more clinically appropriate.

In contrast to Bottenstein, the human oligodendrocyte progenitor cell populations achieved through the protocols of the present invention are virtually pure as to phenotype (First Goldman Declaration ¶ 10). Compare Figure 5B to its control, Figure 5A (Id.). In Figure 5A, the gated single cell represents the false-positive sort incidence (Id.). Such incidences constitute <1% of the frequency of events noted in Figure 5B, indicating >99% purity of the P/CNP2:hGFP-sorted oligodendrocyte progenitor cells (Id.). This can be modulated as a function of sort speed to achieve any desired degree of purity, the trade-off being lower yields as higher degrees of purification are achieved (Id.). By virtue of the high-purity extraction attainable by fluorescence-activated cell sorting, the progenitor cells produced according to the present invention are never exposed to

paracrine factors released by other cells, after removal from tissue (Id.). This permits their maintenance in an undifferentiated and phenotypically-unbiased state, in contrast to the mixed cellular milieu afforded by Bottenstein, in which non-oligodendrocytic and non-glial progenitor-derived phenotypes remain abundant (Id.).

As a result of these considerations, the selective propagation of mitotically-active oligodendrocyte progenitor cells from the neonatal rat brain, as taught by Bottenstein (or Rao), does not predict the successful isolation of mitotic oligodendrocyte progenitor cells from postnatal or adult human brain tissue (see First Goldman Declaration ¶ 11).

The significance of applicants' present invention is apparent from the June 7, 2000, Research/Clinic Update for the National Multiple Sclerosis Society, which accompanied the June 10, 2002, Preliminary Amendment and stated the following:

> Researchers at Cornell University Medical College, supported by the National MS Society, have for the first time isolated cells in the adult human brain that can divide and grow into myelin-making cells and that may ultimately be capable of replacing those damaged in multiple sclerosis.

The isolation of the adult human oligodendrocyte progenitor cell was thus chosen as one of the major MS-related discoveries of 1999 by the National Multiple Sclerosis Society. This work also merited a public affairs release of the Society for Neuroscience, which chose this discovery from thousands of annual research abstracts as one of its most important of the year, with an extensive and detailed release. A subsequent research summary by National MS Society stated:

> Society-supported investigators at Cornell University Medical College reported, for the first time, being able to isolate immature ("progenitor") myelin-making cells in the adult human brain, remove them surgically and transform them, in laboratory dishes, into mature cells capable of making new myelin. This important step may provide a basis for new strategies for repairing damaged myelin in MS.

(attached hereto as Appendix 1). Applicants' work was reported in a number of both regional and national newspapers. Attached is an extensive report of applicants' work in Newsday, then the largest circulation paper in New York City (attached hereto as Appendix 2).

Both the significance and novelty of applicants' present invention are further apparent from its publication in the Journal of Neuroscience (first isolation of human

oligodendrocyte progenitor cells: Roy et al., "Identification, Isolation and Promoter-Defined Separation of Mitotic Oligodendrocyte Progenitor Cells from the Adult Human Subcortical White Matter," *J. Neuroscience* 19:9986-95 (1999) (attached to Third Goldman Declaration as Appendix 6)), Journal of Neuroscience Research (first transplant of cells of human oligodendrocyte progenitor cells into demyelinated brain: Windrem et al., "Progenitor Cells Derived from the Adult Human Subcortical White Matter Disperse and Differentiate as Oligodendrocytes Within Demyelinated Lesions of the Rat Brain," *J. Neurosci. Res.* 69: 966-75 (2002) (attached to Third Goldman Declaration as Appendix 7) (*cover photo*)); Nature Medicine (first transplant of human oligodendrocyte progenitor cells into prenatal brain: Nunes et al., "Identification and Isolation of Multipotent Neural Progenitor Cells from the Subcortical White Matter of the Adult Human Brain," *Nature Medicine* 9:439-447 (2003) (attached to Third Goldman Declaration as Appendix 8) (*cover photo*)); and again Nature Medicine (first transplantation of human oligodendrocyte progenitor cells into congenitally unmyelinated brain: Windrem et al., "Adult and Fetal Human Oligodendrocyte Progenitor Cells Effectively Myelinate Dysmyelinated Brain," *Nature Med.* (2004), *in press*) (attached to Third Goldman Declaration as Appendix 3), which has been accepted for publication (see attachment to Third Goldman Declaration as Appendix 4). These are among the pre-eminent journals in biomedicine. Nature Medicine currently has the highest impact factor of any journal in basic medical research, and its publication of work from the same laboratory twice in a year suggests the importance with which its editors view applicants' present invention and its uses. Thus, those skilled in art recognized that the present invention was a substantial advance in the art over Rao which did not report a means of isolating human oligodendrocyte progenitor cells, let alone such progenitor cells themselves.

Finally, nowhere does Rao teach or suggest an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells where a cyclic nucleotide phosphodiesterase 2 promoter functions in all cells of the enriched or purified preparation.

For all of these reasons, the rejection of the claims under 35 U.S.C. § 102 as anticipated by Rao should be withdrawn.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: December 18, 2003

Michael L. Goldman
Registration No. 30,727

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1304
Facsimile: (585) 263-1600

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Jane C. Wirszyla
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NATIONAL MULTIPLE SCLEROSIS SOCIETY

National Multiple Sclerosis Society
733 Third Avenue
New York, NY 10017-3288
Tel 212 986 3240
1 800 FIGHT MS
Fax 212 986 7981
E-Mail: Nat@nmss.org
www.nmss.org

RESEARCH/CLINICAL UPDATE

January 7, 2000

RESEARCHERS FIND KEY CELLS IN ADULT BRAIN THAT MAY SOMEDAY REPAIR MYELIN IN MS

Summary:

- Researchers at Cornell University Medical College, supported by the National MS Society, have for the first time isolated cells in the adult human brain that can divide and grow into myelin-making cells and that may ultimately be capable of replacing those damaged in multiple sclerosis.
- Although very basic in nature, this research may eventually lead to therapies for MS either through implantation of such cells, or through development of ways of stimulating progenitor cells resident in a person's brain to produce new oligodendrocytes that can repair myelin damaged by MS and possibly restore nerve function.

Details: National MS Society-supported investigators led by Steven A. Goldman, MD, PhD, of Cornell University Medical College, have reported the discovery and isolation of a population of immature ("progenitor") myelin-making cells (oligodendrocytes) in the brains of adult humans. These cells have the potential to repair myelin that has been destroyed by MS, and possibly to aid in the recovery of function.

Reporting in the November 15 issue of *The Journal of Neuroscience*, the investigators describe having found that the oligodendrocyte progenitor cells are surprisingly abundant in adult brain matter, and are capable of dividing to produce new oligodendrocytes. Most adult human brain cells do not divide. This is the first demonstration that such cells can be stimulated to divide and give rise to new oligodendrocytes.

Background

Throughout the 1990s, researchers had been searching for oligodendrocyte progenitor cells in the human brain. Oligodendrocyte progenitor cells had been found in the rat brain in the 1970s and 1980s. Immature oligodendrocytes had been found in human

brain tissue, but none of these had been capable of dividing. Researchers had begun to conclude that oligodendrocyte progenitor cells capable of dividing did not exist in the adult human brain. But by using surgically removed samples of adult human brain tissue, combined with newly developed techniques of molecular cell identification and separation, Goldman and colleagues were able to refute this notion and for the first time, segregate a population of dividing oligodendrocyte progenitors in adult brain.

The study

In this study, reported in the November 15 issue of *The Journal of Neuroscience*, adult human brain cells were obtained from brain matter that was removed from eight patients ranging in age from 24 to 65 years old, who underwent surgery for a variety of disorders. The investigators used a technique they had developed and tested in animal brain cells to separate living progenitor cells from the larger brain cell population.

The investigators identified a discrete population of oligodendrocyte progenitor cells, which they estimated to represent about four percent of the population of cells in the in the white matter of the brain. They then segregated the progenitor cells, and demonstrated that they were capable of dividing, "more or less on demand," says Goldman.

What the Study Means

This study shows that oligodendrocyte progenitor cells exist within the adult human brain and are capable of dividing. Furthermore, this study describes a method for the isolation and actual purification of these cells, potentially in large numbers. This raises the possibility that patients with MS might someday be treated either by transplanting oligodendrocyte progenitor cells, or by stimulating the patients' own oligodendrocyte progenitor cells to divide and produce new cells. Treatments might also be devised that combine elements of both approaches.

Dr. Goldman's team is currently conducting studies to determine whether transplanted oligodendrocyte progenitor cells will be able to produce replacement myelin on nerve fibers whose myelin has been destroyed. Studies will also be needed to determine whether stimulating the growth of new oligodendrocytes from progenitor cells that exist within a patient's brain will remyelinate damaged neurons.

The National MS Society is actively funding these and other efforts to find ways to repair myelin and nerve cells that have been destroyed by multiple sclerosis, with the hope of restoring nerve function.

From: Research Programs Department

SUMMARY OF MS RESEARCH PROGRESS - 1999

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December 10, 1999

This has been another exciting year for MS research. Thanks to funds provided by its chapters and private donors, the National Multiple Sclerosis Society was able to spend a record $22.5 million to support research programs in 1999. Since its founding 53 years ago, the Society has invested more than $260 million to find the cause, treatments and cure for MS.

During the year, our volunteer scientific advisors reviewed 300 MS research proposals and approved 129 as being of high scientific merit and relevance and thus warranting the Society's support. The Society now has over $40 million in current and future commitments to over 300 MS research projects, for which money must be raised.

Significant advances have been made in both laboratory and clinical studies in MS. As the world's largest private supporter of MS research, the Society has been at the core of many of these advances during 1999. Key highlights include:

- In separate Society-supported studies, investigators reported evidence for the possibility that human herpes virus-6 (University of Wisconsin) and the bacterium Chlamydia pneumoniae (Vanderbilt University) may be linked to MS. Further studies are ongoing to determine whether either these or other infectious agents are causal factors in MS, and whether drugs to fight these agents can help MS.

- The first large-scale clinical trial of Copaxone in primary-progressive MS was begun. It will eventually enroll 900 people at 54 centers across the U.S. and Canada.

- Society-supported investigators at Cornell University Medical College reported, for the first time, being able to isolate immature ("progenitor") myelin-making cells in the adult human brain, remove them surgically and transform them, in laboratory dishes, into mature cells capable of making new myelin. This important step may provide a basis for new strategies for repairing damaged myelin in MS.

- The Society launched the Sonya Slifka Longitudinal MS Study. This first study of its kind in the U.S. will collect, on a long-term basis, in-depth information on a national sampling of people with MS in order to address important research questions.

- Society-sponsored researchers at the Mellen MS Center in Cleveland announced results of a study suggesting that individuals with the relapsing-remitting form of MS show progressive loss of brain volume, or atrophy, and that this atrophy may be slowed with interferon beta treatment.

- Investigators at the Weizmann Institute in Israel reported that feeding mice and rats an oral form of Copaxone made their MS-like disease less severe. A large-scale human trial of an oral (pill) form of Copaxone for MS is now being planned. (This drug is currently approved in the U.S. as a daily under-the-skin injection for relapsing-remitting MS.)

- Researchers at Mayo Clinic reported that plasma exchange therapy led to neurologic recovery in about half of 22 people they studied who experienced acute, severe attacks of MS or related disorders and whose neurological deficits were not improved after standard treatment with high-dose steroids.

- As part of the Society's targeted research initiative on gender differences in MS, a small-scale clinical trial of the pregnancy hormone estriol was begun at the University of California at Los Angeles to determine whether it is safe and whether it can control or inhibit MS attacks.

A small-scale clinical trial of a combination of Avonex and Copaxone in relapsing-remitting MS was begun at 5 centers in the U.S., and an international study was launched to compare the effectiveness of Rebif vs. Avonex in relapsing-remitting MS.

- With Society support, doctors at the University of Southern California began a controlled, Phase 2 clinical trial of "T-cell vaccination" in 80 people with secondary-progressive MS. The "vaccine" is designed to specifically kill immune cells that recognize and launch attacks against myelin insulation in the brain and spinal cord.

- Two experimental treatments were brought before the FDA for approval to treat secondary-progressive MS: Novantrone, a potent immune-suppressing chemotherapy drug; and Betaseron, an immune-system modulator currently approved for relapsing-remitting MS. We should learn in 2000 whether either becomes the first approved treatment for a progressive form of MS.

This fruitful year has brought us closer to achieving our goal: to end the devastating effects of multiple sclerosis.

-- Research Programs Department

Beyond the Gray Area

Study finds generating cells in brain's white matter

By Jamie Talan
STAFF WRITER

WHILE RESEARCHERS revel in the recent news that adult brain cells grow and divide in some areas of the gray matter — the brain tissue where neurons do their work — few people have paid attention to the inner workings of the white matter, the brain tissue covering the gray matter.

Dr. Steven Goldman and his colleagues at Weill Cornell Medical College in Manhattan have evidence of young, dividing cells in the white matter in the adult human brain. The hope is to "mass produce" sufficient numbers of these progenitor, or stem cells, for implantation and cell-based therapies to treat multiple sclerosis, stroke, Tay Sachs and other diseases, Goldman said. The study appears in the Journal of Neuroscience.

White matter is a pool of myelin, or insulation, that surrounds the neurons in the gray matter. It is filled with cells that provide nutritional support to the neurons, including oligodendrocytes and androcytes. The classic lesions identified in patients with multiple sclerosis are found in white matter. Also, one-third of stroke victims suffer lesions in this tissue.

Newsday Photo / Patrick Andrade

Dr. Steven Goldman, of the Department of Neurology at Weill Cornell Medical College in Manhattan, studied the brain's white matter.

The researchers have developed a method to isolate these progenitor cells by linking them to a gene for a jellyfish fluorescent protein and using a cell-sorting device to separate them from other types of brain cells.

With this pure population of progenitor cells in hand, Goldman said, it would be possible to develop specific techniques to be used after a brain trauma to replace this insulating material and, in theory, fix the brain's transmission problems. (The myelinated axons are the brain's version of telephone wire, long projections that send signals from cell to cell and enable neurons to communicate.)

Goldman, a neurologist, working with his colleague, Neeta Ray, isolated the newly dividing cells from live tissue taken from epilepsy patients and others undergoing brain surgery or biopsy.

Oligodendrocytes are necessary to make myelin, the insulating sheath that surrounds nerve cells that make communication possible. In multiple sclerosis, oligodendrocytes are inflamed or die as the nerve cells' myelin are shredded.

Astrocytes, support cells that provide metabolic support for neurons, are known to grow and divide, but it was always believed that oligodendrocytes, like neurons, do not re-populate. And while scientists have known that the oligodendrocytes are the cells targeted in MS, the immune system disease has always puzzled researchers because the symptoms — tingling in the extremities, tiredness and loss of normal movement — wax and wane. The white matter lesions seem to get better, as well, and it has never been clear how or why axons re-myelinate.

Goldman, a researcher who started his career studying neurogenesis in canary brains, was convinced that there must be a population of oligodendrocyte-progenitor cells that was helping the adult brain heal itself — at least temporarily.

Working side by side with neurosurgeons, Goldman was able to amass snippets of brain tissue from dozens of patients.

By culturing the tissue, the researchers were able to sort out the oligodendrocytes and watch them grow and divide.

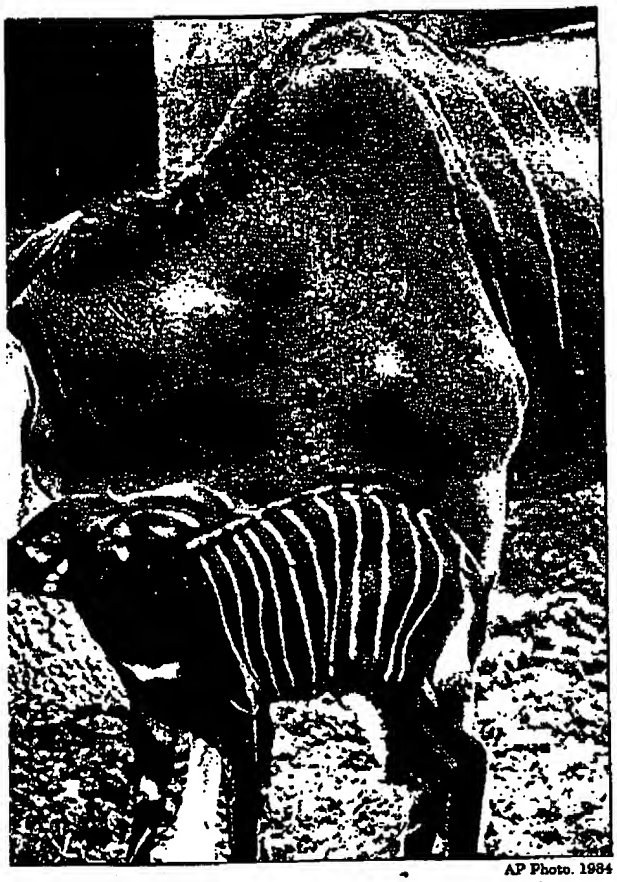
In more recent, unpublished work conducted to

See BRAIN on C6

DID YOU KNOW?

By Kathy Wollard

REMEMBER "You're only as young as you think you are"?



AP Photo. 1984

antelope, at the Cincinnati Zoo in 1984, was transferred as an
l antelope in an effort to preserve the rare species.

g vs. Extinction

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coming the problems of breeding in captivity, including the obvious fact that in a lab scientists have to deal with the problem of animals who have been removed from their natural surroundings.

George Amato of the Wildlife Conservation Society's Science Resource Center and the Bronx Zoo in New York City, said cloning is one tool that can be used to save rare animals, but he's not enthusiastic about the method in his own research.

Amato is using molecular genetic techniques to help conserve endangered species and, like Dresser, maintains a frozen zoo of sorts — a collection of frozen DNA. Amato said that when rare animals become difficult to observe through traditional methods because they can't be found, DNA helps the scientists in their research.

"We maintain frozen DNA from animals from hundreds of species, most of which are endangered," Amato said. His frozen DNA collection includes the the black rhinoceros from Tanzania, endangered yellow-shouldered Amazon parrots from Venezuela and American crocodiles from Belize.

Despite his reluctance to use cloning, Amato said there is a place for it.

"I do believe it has an application for very specific cases," he said. "The panda is probably a reasonable case. I think that we have some responsibility to the things living we are driving to extinction."

Mind Over Brain's White Matter

BRAIN from C5

test whether the cells are functional, the investigators implanted the tissue containing the oligodendrocytes into animals with a demyelinating disease.

The new tissue developed into oligodendrocytes and made myelin protein, but whether they line up along the axon is still not known, Goldman said.

"It may one day be possible to activate a person's endogenous stem-cell population and generate these cells on demand," Goldman said.

Another option, he added, is to purify these cells and insert them into the white matter of patients. For example, doctors could inject the progenitor-oligodendrocytes into MS plaques or into the stroke lesions to trigger re-myelination.

Goldman believes that the population of stem cells in white matter may be far easier to identify, purify and manipulate than the small number of progenitor cells found in the subventricular zone of the gray matter deep in the brain.

He said there are 10 times as many white matter support cells, also called glia, as neurons in the brain, and that as much as 4 percent of the cells in the white matter may be progenitor cells.

The neurologist also believes that it will be possible to insert a single gene into the progenitor cells, such as the gene that is abnormal in Tay-Sachs.

This would restore the myelin, which is damaged and leads to early death in childhood. Goldman also believes that stroke will also be a good model for this modern treatment.

"The possibility to do these experiments is here, now," Goldman said.

He thinks this material could be in human trials within three years.

"It's one thing to talk about new brain cells. It's another to be able to use them for treatment," Goldman said.

Goldman's group collaborates with Peter Braun and Michel Gravel of McGill University in Montreal, who cloned the oligodendrocyte-specific protein used in the studies to identify the progenitor cells.

The rush to tap into neurogenesis — the growth of brain cells — is fraught with problems.

As it turns out, brain growth isn't always good, and it isn't always normal. A number of labs are beginning to find that growing cells in a test-tube can lead to a population of abnormal cells. In other words, the cells are growing waywardly like cancers and lose their neuronal functional capacity.

Goldman's work bypasses this problem by finding an abundance of progenitor cells rather than helping a few cells grow and multiply.

Sky Watch

ONE OF MY FAVORITE days of the year is right around the corner. I'm talking about the first day of winter. The reason is the winter solstice, which occurs this year at 2:44 a.m. Dec. 22 on the East Coast. The winter solstice marks the moment that the sun reaches its southernmost position over our planet and begins its journey northward. To an observer on Earth, the day marks the sun's lowest position in the midday sky, and the beginning of its climb once again.

It all happens because our planet's equator is tipped by about 23.5 degrees to the plane of our orbit around the sun. This means that, during this time of year, the Earth's Northern Hemisphere tilts away from the sun, causing the sun's rays to shine down on us at a shallow angle. Six months and half an orbit later, our planet's tilt aims the Northern Hemisphere toward the sun, causing the sun's rays to shine down on us at a more direct angle.

"solstice" originates in antiquity, coming from two Latin words — "sol" (meaning "sun") and "sistere" (meaning "to stand still").

It is at the winter solstice that the sun's southerly drop seems to end, the sun "stands still," and the star that gives life to planet Earth begins its ascendancy once again. From this moment on, the days become longer, the sun appears higher, and the greens of life gradually return to the Northern Hemisphere of Earth. And not a moment too soon, either!

DENNIS MAMMANA / COPLEY NEWS SERVICE